[ID: 225] Anti-virulent properties of a phage-encoded depolymerase against A. baumannii K2 capsular type

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Capsular structures are seen as a universal virulence trait among gram-negative bacilli but sill poorly studied in Acinetobacter baumannii. Recent reports suggest that capsule structures are involved in evading or overwhelming microbial defenses and macromolecular antibiotics. The fact that at least 106 capsular types exist in A. baumannii may reflect the sophisticated and diverse protective mechanisms developed by this pathogen. In this study, we isolated a 93,641-bp phage infecting A. baumannii K2 capsular type and cloned its tail-associated depolymerase (B3gp42). The enzyme showed to digest extracted exopolysaccharides in a wide range of pH values (5 to 9), ionic strengths (0 to 500 mM) and temperatures (20 to 70°C). Additionally, the enzyme is stable for at least 2 years. To assess the anti-virulence properties, the B3gp42 was tested against K2 strain using i) a human alveolar epithelial model, ii) a Galleria mellonella caterpillar model and finally ii) human blood (serum and neutrophil killing). In the human lung epithelium, B3gp42 demonstrated to be non-toxic and able to reduce the K45 strain virulence in a time-dependent manner. Complementary studies performed in vivo showed that B3gp42 was able to rescue larvae infected with either K2 strain pretreated with B3gp42 for 2 hours or with B3gp42 administered 30 min after bacterial inoculation. Additionally, we show that the B3gp42 could make the K2 strain fully susceptible to human serum and neutrophil killing, reducing the pathogen below detection limit (<10 CFU/mL). Overall, we show for the first time that the capsule is an important virulence factor of A. baumannii and that capsule removal via B3gp42 activity helps the host immune system to combat the bacterial infection. We conclude that capsular depolymerases represent a high therapeutic potential against A. baumannii drug-resistant infections.